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      (FILE 'HOME' ENTERED AT 13:01:29 ON 30 OCT 2001)

      INDEX 'ADISALERTS, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI,
      BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO,
CABA,
      CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB,
      DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 13:01:43 ON
      30 OCT 2001
                 SEA PPVWF OR VWF PROPEPTIDE OR PROVWF OR PRO-VWF
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                 1   FILE ADISALERTS
                 0*  FILE ADISNEWS
                65   FILE BIOSIS
                 6   FILE BIOTECHABS
                 6   FILE BIOTECHDS
                49   FILE BIOTECHNO
                 5   FILE CANCERLIT
                64   FILE CAPLUS
                 3   FILE CONFSCI
                 1   FILE DDFU
                12   FILE DGENE
                 1   FILE DRUGU
                 2   FILE EMBAL
                65   FILE EMBASE
                25   FILE ESBIOBASE
                 2   FILE GENBANK
                10   FILE LIFESCI
                65   FILE MEDLINE
                29   FILE PASCAL
                 1   FILE PROMT
                50   FILE SCISEARCH
                17   FILE TOXLIT
                17   FILE USPATFULL
                 4   FILE WPIDS
                 4   FILE WPINDEX
L1               QUE PPVWF OR VWF PROPEPTIDE OR PROVWF OR PRO-VWF
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      FILE 'BIOSIS, EMBASE, MEDLINE, CAPLUS, SCISEARCH, BIOTECHNO, PASCAL,
      ESBIOBASE, TOXLIT, USPATFULL, DGENE, LIFESCI, BIOTECHDS, CANCERLIT,
      WPIDS, CONFSCI, EMBAL, ADISALERTS, DRUGU, PROMT' ENTERED AT 13:04:32 ON
      30 OCT 2001
L2             0 S (PPVWF OR VWF PROPEPTIDE OR PROVWF OR PRO-VWF) (10A) (CELL
FR
L3            17 S (PPVWF OR VWF PROPEPTIDE OR PROVWF OR PRO-VWF) AND CELL FREE
L4             5 DUP REM L3 (12 DUPLICATES REMOVED)
L5            19 S (PPVWF OR VWF PROPEPTIDE OR PROVWF OR PRO-VWF) (3A)
RECOMBINA
L6             4 DUP REM L5 (15 DUPLICATES REMOVED)
L7             0 S (PPVWF OR VWF PROPEPTIDE) (3A) RECOMBINANT
L8             1 S (PPVWF OR VWF PROPEPTIDE) (10A) RECOMBINANT
L9             3 S (PPVWF OR VWF PROPEPTIDE) (10A) (TREAT? OR PHARMACEUTICAL)
L10          127 S PPVWF OR VWF PROPEPTIDE
L11           36 DUP REM L10 (91 DUPLICATES REMOVED)
L12           14 S L11 AND RECOMBINANT

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L4 ANSWER 4 OF 5 USPATFULL
AN 93:82738 USPATFULL
TI Method for producing factor VIII:C-type proteins
IN Kaufman, Randal J., Boston, MA, United States
Adamson, S. Robert, Chelmsford, MA, United States
PA Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)
PI US 5250421 19931005
AI US 1992-824765 19920117 (7)
RLI Continuation of Ser. No. US 1988-260085, filed on 19 Oct 1988, now abandoned which is a continuation-in-part of Ser. No. US 1986-816031, filed on 3 Jan 1986, now abandoned And Ser. No. US 1996-942338, filed on
16 Dec 1996, now abandoned And Ser. No. US 1987-34882, filed on 6 Apr 1987, now abandoned And Ser. No. US 1987-68865, filed on 2 Jul 1987, now
abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Low, Christopher S. F.
LREP Berstein, David, DesRosier, Thomas J., Eisen, Bruce M.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 997
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An improved method for producing Factor VIII:c-type proteins is disclosed which involves culturing mammalian cells which are capable of expressing the protein. In accordance with this invention the cells are cultured in a medium containing an effective amount of a substance comprising (a) von Willebrand Factor-type protein, (b) a phospholipid or
phospholipid mixture, or a mixture of (a) and (b).
SUMM For example, truncated forms of human VWF which may be used in the practice of this invention include (i) .DELTA.**pro VWF**
, which lacks the "pro" sequence of VWF; (ii) .DELTA.mature VWF, which comprises the "pro" sequence without the mature sequence; and, (iii) VWF-5'-Sac, which comprises the sequence of **pro-VWF**
from the N-terminus to the 5' Sac I restriction site and includes the "pro" portion of VWF as well as. . . . amino acid positions 23 through Arg-763 and the "mature" protein spans amino acid positions 764 through 2813. A cDNA encoding .DELTA.**pro VWF** may be prepared

J.BC. 264(11): 6017-6020 (1989)

L3 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2
AN 1998:298723 CAPLUS
DN 128:304189
TI The effects of sex steroids on plasma levels of marker proteins of endothelial cell functioning
AU Van Kesteren, P. J. M.; Kooistra, T.; Lansink, M.; Van Kamp, G. J.; Asscheman, H.; Gooren, L. J. G.; Emeis, J. J.; Vischer, U. M.; Stehouwer, C. D. A.
CS Department Andrology, Academic Hospital, Vrije Universiteit Amsterdam, Amsterdam, Neth.
SO Thromb. Haemostasis (1998), 79(5), 1029-1033
CODEN: THHADQ; ISSN: 0340-6245
PB F. K. Schattauer Verlagsgesellschaft mbH
DT Journal
LA English
AB The authors studied male-to-female (M.fwdarw.F) and female-to-male (F.fwdarw.M) transsexuals who, for 4 mo, received cross-sex **treatment** with, resp., ethinylestradiol and cyproterone acetate, and with testosterone esters. The authors assessed the effects of **treatment** on blood plasma levels of tissue-type plasminogen activator (tPA), von Willebrand factor (vWF), **vWF-propeptide** (vWF: AgII) and big-endothelin-1 (big-ET-1), 4 proteins that are markers of endothelial cell functioning. The authors also measured urokinase-type plasminogen activator (uPA) and plasminogen activator inhibitor-type 1 (PAI-1), which may not be endothelium-derived but share major clearance pathways with tissue-type plasminogen activator (tPA). In M.fwdarw.F plasma levels of tPA (-4.4 ng/mL), big-ET-1 (-0.8 pg/mL), uPA (-0.5 ng/mL) and PAI-1 (-26 ng/mL) decreased. The level of vWF increased (+24%), while vWF: AgII did not change. In F.fwdarw.M transsexuals, levels of big-ET-1 increased (+0.4 pg/mL), while tPA, uPA, and PAI-1 did not change. In this group vWF decreased (-14%), but vWF:AgII did not chang. Estrogens and androgens have clear effects on plasma levels of endothelial marker proteins. The mechanisms behind these effects are complex and appear to involve both altered secretion (big-ET-1) and processing and/or clearance (vWF and possibly tPA). Therefore, effects of hormones on the levels of endothelial marker proteins do not necessarily reflect changes in endothelial cell functioning, at least with regard to changes in vWF level assocd. with the oral administration of high doses of ethinylestradiol and cyproterone acetate to healthy men and the parenteral administration of testosterone to healthy women.

3 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 3
AN 1998:614625 CAPLUS
DN 129:229154
TI Quantitative analysis of von Willebrand factor and its propeptide in plasma in acquired von Willebrand syndrome
AU Van Genderen, Perry J. J.; Boertjes, Ria C.; Van Mourik, Jan A.
CS Department Hematology, Hospital Dijkzigt, University Rotterdam, Rotterdam, 3015 GD, Neth.
SO Thromb. Haemostasis (1998), 80(3), 495-498
CODEN: THHADQ; ISSN: 0340-6245
PB F. K. Schattauer Verlagsgesellschaft mbH
DT Journal
LA English
AB Measurement of the von Willebrand factor (**vWF**) **propeptide**, also known as von Willebrand antigen II, was suggested to be helpful in the discrimination of congenital von Willebrand disease type I from type 2 and in assessing the extent of activation of the endothelium. The authors performed a quant. anal. of mature vWF and its propeptide in plasma in patients with acquired von Willebrand syndrome (AvWS). Mature vWF levels were lower in AvWS as compared with normal individuals (13.4 vs. 35.6 nM). Propeptide levels were higher in AvWS (11,4 vs. 4.7 nM) probably reflecting a compensatory increase in vWF synthesis or increased perturbation of the endothelium in AvWS. After **treatment** with 1-deamino-8-D-arginine vasopressin (DDA-VP), propeptide and mature vWF levels rose 5-fold in AvWS, whereas propeptide were not altered by the infusion of a vWF conc. or **treatment** with high dose i.v. Igs, indicating that plasma propeptide levels are a reliable reflection of vWF synthesis. Measurement of propeptide may provide addnl. information in AvWS as to whether decreased levels of mature vWF in the circulation are due to a decrease in synthesis or due to an acce

L5 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 12
AN 1991:426685 CAPLUS
DN 115:26685
TI Immunological detection of propolypeptide of von Willebrand factor on platelet surface
AU Hashimoto, Keiko; Usui, Tomoko; Sasaki, Kenichi; Fujisawa, Tomoyuki; Sekiya, Fujio; Takagi, Junichi; Tsukada, Toshiyasu; Saito, Yuji
CS Dep. Biol. Sci., Tokyo Inst. Technol., Tokyo, 152, Japan
SO Biochem. Biophys. Res. Commun. (1991), 176(3), 1571-6
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB It was found previously that the propolypeptide of von Willebrand factor (**pp-vWF**) obtained from platelets binds to type I collagen. Two types of evidence were found to show that it is also present on the surface of resting platelets: (1) the antibody against **pp-vWF** bound to the surface of platelets, and (2) the antibody induced aggregation of platelets. The binding of the antibody and the antibody-induced aggregation of platelets were inhibited in a dose-dependent manner by Fab fragment of the antibody. Platelets from von Willebrand disease patients bound less of the antibody and responded

L5 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 13
AN 1991:444438 CAPLUS
DN 115:44438
TI Monoclonal antibodies that inhibit binding of propolypeptide of von Willebrand factor to collagen. Localization of epitopes
AU Fujisawa, Tomoyuki; Takagi, Junichi; Sekiya, Fujio; Goto, Akira; Miake, Fumio; Saito, Yuji
CS Fac. Biosci. Biotechnol., Tokyo Inst. Technol., Tokyo, 152, Japan
SO Eur. J. Biochem. (1991), 196(3), 673-7
CODEN: EJBCAI; ISSN: 0014-2956
DT Journal
LA English
AB It was reported previously that the bovine propolypeptide of von Willebrand factor (**pp-vWF**) binds to type I collagen. To det. the collagen-binding sites of **pp-vWF**, monoclonal antibodies (mAbs) were generated against bovine **pp-vWF**. One mAb, designated TC8, very strongly inhibited the binding of **pp-vWF** to type I collagen; 3 other mAbs, designated TC2, TC6, and TC7, exhibited moderate inhibition. Competition between the mAbs for binding to intact **pp-vWF** revealed that the epitope for TC8 was structurally independent of that for TC6 and TC7. To det. directly the location of the epitope for each mAb on the bovine **pp-vWF** mols., the reactivity of mAbs was tested by immunoblotting toward peptide fragments obtained by digestion with lysyl endopeptidase. TC2 and TC8 recognized a fragment of 21-kDa mol. wt., whereas TC6 and TC7 recognized a distinct fragment of 18 kDa. These 2 fragments were purified to homogeneity and their N-terminal amino acid sequences were detd. Comparing these sequences with the sequence of human **pp-vWF**, the locations of these fragments in the primary structure were estd. to be Phe-570-Lys-682 for the 21-kDa fragment and Glu-281-Lys-375 for the 18-kDa fragment. These data suggest that **pp-vWF** contains at least 2 collagen-binding sites which lie within or close to the regions between Phe-570-Lys-682 and

09/424,413

L5 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 14
AN 1989:190017 CAPLUS
DN 110:190017
TI Inhibition of platelet-collagen interaction by propolypeptide of von Willebrand factor
AU Takagi, Junichi; Sekiya, Fujio; Kasahara, Kohji; Inada, Yuji; Saito, Yuji
CS Dep. Biol. Sci., Tokyo Inst. Technol., Tokyo, 152, Japan
SO J. Biol. Chem. (1989), 264(11), 6017-20
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB A collagen-binding glycoprotein was isolated from human platelets by using affinity chromatog. of immobilized collagen. Based upon characterizations of this protein, it was confirmed to be identical to the propolypeptide of von Willebrand factor (**pp-vWF**), which is also called von Willebrand antigen II. The characteristics investigated were mol. wt., existence of carbohydrate chains, and the N-terminal amino acid sequence. The **pp-vWF** has strong affinity to collagen and inhibits collagen-induced aggregation of human platelets at a concn. as low as 2 .mu.g/mL even in the presence of plasma. This inhibitory effect is specific for collagen-induced aggregation since it does not inhibit aggregation of platelets induced by other agonists such as ADP, arachidonic acid, platelet-activating factor, ionophore A 23187, and ristocetin. As **pp-vWF** is quickly released from platelets upon activation by various agonists, it is possible that **pp-vWF** functions as a repressor for excess platelet aggregation induced by collagen and constitutes a neg. feedback mechanism.
Considering the fact that mature vWF supports platelet adhesion to subendothelium, these observations suggest that the propeptide portion and the mature protein could have opposing effects on hemostasis.